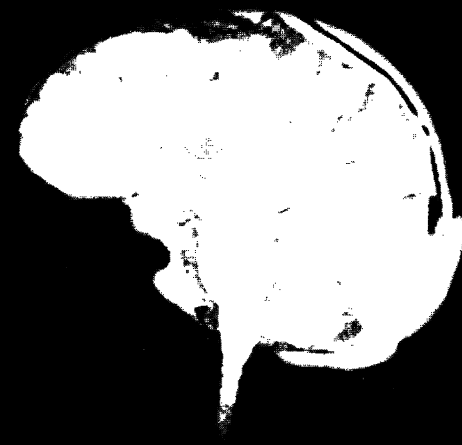
NEUROLOGY

FROM BASICS TO BEDSIDE



Neurology

THIS SPECIAL ISSUE of THE WESTERN JOURNAL OF MEDICINE takes us from bench to bedside, from cradle (and before) to grave, from diagnosis to treatment, from training to practice. We are taken from the common to the unimaginable, from the past to the future, from theoretical and practical to ethics and policy. Conditions may be acute or chronic and may require intensive care or rehabilitation.

Stephen Hauser, MD, Chair of the Department of Neurology at the University of California, San Francisco, School of Medicine, has been the inspired and inspiring special editor, a visionary leader, and persuader of his distinguished authors. We readers, patients, families, policy makers, and the public are grateful.

LINDA HAWES CLEVER, MD

Introduction

NEUROLOGY HAS ENTERED a new era. Long considered an intellectually rich but therapeutically impoverished discipline, neurologists have traditionally functioned as prestidigitators in the spectacle of medicine, capable of astonishing displays of anatomic localization, pathologic inference and diagnosis, but with services that are ultimately limited to the education of patients or referring physicians. Medical students frequently have been heard to comment that neurology is an interesting but depressing specialty.

In the mass media or in literature, also, we neurologists tend to be treated unkindly. The most frequent image is that of the mad scientist, brilliant but deranged, the villain who exploits neuroscience for evil or twisted purposes: Dr Frankenstein; or Frank MacLeary, cadaveric organ dealer in Robin Cook's *Coma*. On occasion, a more sympathetic image presents neurologists as lovable but disheveled nerds, socially infantile, well-meaning, but ultimately ineffective. We suspect that orthopedists would not have tolerated the public image that neurologists have endured in silence for so long.

I hope that this issue of THE WESTERN JOURNAL OF MEDICINE will contribute in a small way to a changing perception of neurology. Each of three sections will focus on a different aspect of progress and change in the field. A remarkable and distinguished group of contributors will guide readers through this rapidly changing terrain.

Within the past decade, molecular biology has transformed neurology more dramatically and more rapidly than even its most visionary proponents would have dared to predict. Genetic linkage approaches have resulted, as of this writing, in the identification of more than 50 neurologic disease genes and in the chromosomal localization of several hundred more. The genes responsible for some of the most common and mysterious nervous system diseases, including Duchenne-type muscular dystrophy (dystrophin), myotonic dystrophy (CTG repeat 3′ of myotonin), Huntington's disease (huntingtin), Charcot-Marie-

Tooth disease type 1A (PMP-22), and neurofibromatosis type 1 (neurofibromin) have been identified.

Equally exciting is the potential to apply linkage strategies to genetically complex neurologic disorders. In contrast to the single gene disorders discussed here, genetically complex diseases may be polygenic in origin, such as those due to the effects of multiple unlinked genes, or have both a genetic and an environmental component to their pathogenesis. The most spectacular recent discovery in this area has been the demonstration of the apolipoprotein E (apo E) gene effect on Alzheimer's disease. The human apo E gene and protein has four major alleles or forms. The presence of the E-4 allele that occurs normally on approximately 15% of chromosomes is a clear risk factor for sporadic—and some late-onset familial—forms of Alzheimer's disease. How the E-4 allele influences the appearance of Alzheimer's disease is not entirely clear, but it may injure neurons by interacting with the β-amyloid peptide, resulting in neuritic plaque formation, or by destabilyzing the cytoskeletal τ protein and facilitating the development of neurofibrillary tangles.

In the first section of this special issue, entitled "Discovery," several areas of important breakthroughs in the understanding of neurologic diseases are highlighted. The 1990s have been designated by Congress as "The Decade of the Brain." We thus begin with a discussion of the goals of the "Decade of the Brain" project, achievements to date, and prospects for the future. We follow with a summary of advances and challenges facing neurogenetics and with discussions of how growth factors work in the nervous system and the prospects for selective immune manipulation and gene therapy. The spectacular story of prions, a novel genetic and infectious cause of disease, is discussed, as is the molecular understanding of the biology of alcohol abuse. The selection includes a glimpse into developing neuroimaging techniques that permit the study of human brain function in vivo.

The second section, "Therapy," deals with practical aspects of therapy for neurologic diseases. Here we have focused on five categories of nervous system disorders—stroke, multiple sclerosis, headache, Parkinson's disease, and epilepsy—commonly encountered in medicine. For each, important therapeutic developments have raised or are in the process of raising the standard of care that is possible.

The third section, "The New Era," is intended to challenge readers in different ways. Some areas that are explored do not permit complete objectivity, and we apologize in advance for any unintended offense that readers with a different perspective may find on reading this section. The authors explore the place of neurology in the medical world and by extrapolation the ideal number of practitioners that are needed in this specialty. Contributions on neuroimaging, education, neurorehabilitation, and biotechnology are offered. The final chapter attempts to summarize the future clinical role of neurologists in an integrated health care delivery system.

Concern with the size of our specialty is not unique to neurology. It is common to most medical enterprises that are attempting to fit into an evolving health care system. The physicist Freeman Dyson,* writing about the importance of size in nature, observed the following:

> To survive, an animal has not only to be of the right size for the functioning of its internal anatomy. It has also to be of the right size to form a stable community with the bigger and smaller creatures on which it is dependent. In the natural ecology of living creatures, the overwhelming majority of successful animals are small, but the few large animals tend to dominate the landscape. The large animals have an ecological importance that is out of proportion to their numbers. And so it is also in science. The vast majority of successful scientific enterprises are small, but the big enterprises also have an essential role to play. And the big enterprises tend to dominate the political and educational milieu within which the small enterprises must learn to survive. Out of this dominance of the big enterprises arise the central questions of scientific ecology. How should the balance between big and small be maintained? How big is too big and how small is too small? How can we launch large projects without creating political pressures that endanger the integrity of science? . . . We cannot calculate from general principles the optimal size of a scientific project, any more than we can calculate from general principles the optimal size of an elephant or a whale. Every scientific project is unique, just as every species of animal is unique. The purpose of the science of ecology is not to calculate the sizes of elephants and whales but to understand the conditions under which elephants and whales can flourish.

As in science, so it is for medicine. For neurology to flourish, it must do so by creating a proper fit for itself in the modern health care system, in the increasingly competitive world of basic neuroscience research, and in a society whose resources are strained. Neurology must demonstrate the value of its clinical services to patients with neurologic disease, define its role in the education of generalists, and justify its continuing leadership in disease discovery. The authors and I hope that in this special issue, we have conveyed to readers a sense of the excitement, ferment, and promise of the field.

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**On Being the Right Size: Reflections on the Ecology of Scientific Projects,* 1988. Reprinted in *From Eros to Gaia,* Pantheon Books, New York, NY, 1992.